TAB 2 – DRAFT PANEL QUESTIONS

1. The primary rupture rate information comes from Inamed's Core Study which involves complete 3-year data and partial 4-year data. The partial 4-year data includes only physician follow-up. MRI cohort data were captured at the 1-year and 3-year timepoints. The following information is currently known regarding the rupture rate from Inamed's Core Study data:

   - For the MRI Cohort (approximately one-third of the Core Study patients who had serial MRI at years 1 and 3 following implantation), by-patient, total rupture rates (silent + symptomatic) through 4 years are 3.4% for augmentation, 20.5% for reconstruction, and 10.9% for revision.

   - For the Non-MRI Cohort (approximately two-thirds of the Core Study patients who did not undergo MRI), the by-patient, total rupture rates (silent + symptomatic) through 4 years are 1.1% for augmentation, 4.9% for reconstruction, and 1.7% for revision.

   Inamed also provided rupture rate information from supplemental sources, such as the Danish Registry, the literature, and the Adjunct Study.

   To estimate the rupture rate over the expected lifetime of the device, Inamed constructed a hypothetical curve extrapolating the rupture rate observed in the Core Study to estimate a by-implant 10-year rupture rate of 14% across all indications. The sponsor's approach is based on the following assumptions: that the silent rupture rate in the Non-MRI Cohort can be predicted from the MRI Cohort; that averaging the increase in rupture rate at yearly intervals is appropriate; that the rate at which rupture occurs over time is constant; and that it is appropriate to average together the rupture rate for the augmentation, reconstruction and revision patients. As noted in our review memo and presentation, there are other models which could be selected, which lead to higher estimates of rupture.

   Considering the rupture information provided in their submission, and given that the majority of ruptures for silicone gel-filled breast implants are silent, please discuss whether Inamed has adequately characterized the rupture rate and how this rate changes over the expected lifetime of their device.

2. Considering the new additional information presented on consequences of rupture from the Core Study and supplemental sources, please discuss whether Inamed has adequately characterized the consequences of rupture for their device with regard to:

   a. the frequency of observed intracapsular gel, extracapsular gel, and migrated gel, as well as the destination of the migrated gel

   b. the local health consequences of patients with ruptured implants

   c. the incidence, prevalence, and timing of silent ruptures that progress to symptomatic ruptures

d. the incidence, prevalence, and timing of intracapsular ruptures that progress to extracapsular ruptures.

3. Inamed's proposed labeling includes recommendations for: (1) the method and frequency of screening for silent rupture; (2) clinical management of suspicious and confirmed intracapsular and extracapsular rupture; and (3) potential health consequences of extracapsular and migrated gel. Please discuss the appropriateness of these recommendations and the extent to which the proposed labeling is supported by the available information.

4. At the October 2003 Panel meeting, the Panel recommended that patient follow-up after explantation, rupture rate data, data on children of women with silicone gel breast implants, and connective tissue disease data be collected in postapproval studies. To address these issues, Inamed proposes the following:

   First, Inamed proposes continuation of their existing Core Study with yearly physician follow-up through 10 years, with MRIs continuing at years 3, 5, 7, and 9. Safety and effectiveness data will be collected as in the Core Study with one exception. Inamed proposes to remove the requirement to complete the QoL questionnaire at years 6, 8, and 10. Patients who are explanted without receiving replacement implants will be followed via telephone survey, and will no longer undergo MRI screening for silent rupture. Their postapproval study will not collect data on children of women with breast implants.

   Second, Inamed proposes using the Danish Registry or 3rd party organizations, such as the NIH, to collect additional data to address the October 2003 Panel concerns. However, Inamed did not describe any specific plans for using these sources of information.

   Third, Inamed proposes to link their current voluntary registry, which collects baseline and demographic data, but no postoperative information, to their rupture warranty program.

   Please discuss whether the plans are adequate to address the issues previously noted by the Panel or any other postapproval concerns that you might have.

5. Based on your answers to the questions 1-4 above, as well as the other safety data/information and preclinical testing presented at the October 2003 Panel meeting, please discuss whether you believe that there is reasonable assurance that this device is safe[1] over its expected lifetime for the proposed indications of breast augmentation, reconstruction, and revision. With respect to rupture, you should consider that most ruptures are silent and that there is difficulty in ensuring routine MRI examination for women with breast implants. You should also consider data from revision patients as a continuum for patients originally undergoing breast augmentation or reconstruction.

[1] 21 CFR 860.7(d)(1) states that there is a reasonable assurance that a device is safe when it can be determined that the probable benefits to health from use of the device for its intended uses, when accompanied by adequate instructions for use and warnings against unsafe use, outweigh any probable risks.